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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,557	07/16/2001	Takahiko Ishiguro	Q65441	6024

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EXAMINER	
SAKELARIS, SALLY A	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/904,557	ISHIGURO ET AL.	
	Examiner	Art Unit	
	Sally A. Sakelaris	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/29/2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This action is written in response to applicant's correspondence submitted 7/29/2005. Claims 13, 14, and 16 have been amended, claims 1-12 have been canceled, and no claims have been added. Claims 13-16 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as necessitated by applicant's amendments to the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is FINAL.**

Response to Arguments

Applicant's arguments with respect to claims 13-16 have been considered but are moot in view of the new ground(s) of rejection that are required for applicant's newly amended claims.

Claim Interpretations

Applicant should note that "a selected portion of" will be interpreted as any portion of any DNA sequence that has been selected by virtue of amplifying it. Furthermore, the newly recited limitation of "corresponding" will be interpreted as two sequences, which in this case a DNA sequence that corresponds to the RNA sequence that codes for its translation of the sequence encoded thereby.

THE FOLLOWING ARE NEW REJECTIONS NECESSITATED BY APPLICANT'S AMENDMENTS TO THE CLAIMS

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 13 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Davey et al. (US Patent 5,409,818).

With regard to claims 13 and 16 Davey et al. teach a method for determining whether a selected DNA molecule encodes a gene expression region which in this case is a 92 bp segment of the gag portion of the HTLV-III genome, the causative agent of AIDS(Col. 12 lines 33-35), said method comprising:

(A) obtaining RNA transcripts from an organism(ultimately HIV-1 virus, also *E.Coli*, Col. 11 line 50) which comprises said selected DNA molecule,

(B) screening said RNA transcripts for an RNA transcript corresponding to a selected portion of said selected DNA molecule, wherein the nucleotide sequence of said selected portion of said selected DNA molecule is known, to thereby determine whether said selected portion of said selected DNA molecule encodes a gene expression region such as the 92 bp segment of the gag portion of the HTLV-III genome(Col. 12 lines 33-35), wherein said screening comprised:

(i) amplifying the RNA transcripts using a first oligonucleotide primer and a second oligonucleotide primer, wherein said first primer is complementary to a sequence of at least 10 continuous nucleotides located at or near the 3'-end of said selected portion of said selected portion of said selected DNA molecule, and said second primer is homologous to a sequence of at least 10 continuous nucleotides located at or near the 5'-end of said selection portion of said selected DNA molecule(See Figure 1 and Col. 5 lines 14-25, Col. 6 lines 19-68 for example), and

(a) forming a RNA-DNA duplex comprising one of said RNA transcripts and a complementary DNA molecule adhered thereto, said duplex is formed by synthesizing a first DNA molecule complementary to at least a portion of one of said RNA transcripts using (1) said first oligonucleotide primer to prime synthesis of said first DNA molecule, (2) RNA-dependent DNA polymerase and (3) one of said RNA transcripts as a template, to thereby form an RNA-DNA duplex as can be seen in Figure 1 and Col. 5 lines 27-35 for example.

(b) preparing a single stranded DNA molecule from said RNA-DNA duplex of (e) by hydrolyzing the RNA transcript of said RNA-DNA duplex using ribonuclease H(Col. 8 lines 20-33 for example).

(c) forming a doubled-stranded DNA molecule comprising the single-stranded DNA molecule of (f) and a complementary DNA molecule thereto, said doubled-stranded DNA molecule is formed by synthesizing a second DNA molecule complementary to at least a part of said single-stranded DNA molecule of (f) using (1) said second oligonucleotide primer to prime the synthesis of said second DNA molecule, wherein said second primer further comprises an RNA-transcriptable promoter sequence at its 5'-end, (2) DNA-dependent DNA polymerase, and (3) the single-stranded DNA molecule of (f) as a template, to thereby form a double stranded DNA molecule as can be seen in Figure 1 and further in Col. 4 lines 10-15.

(d) forming an RNA transcription product from said double-stranded DNA molecule of (g) using RNA polymerase, wherein RNA transcription is primed from the RNA-transcriptable promoter sequence(Col. 7 lines 28-47 for example).

(e) repeating steps (a) to (d) using said RNA transcription product of (d) as a template for the formation of the RNA-DNA duplex of (a)(Col. 19 claim 1(C)).

(ii) detecting an amplification product of (i) corresponding to said selected portion of said DNA molecule, to thereby screen said RNA transcripts for an RNA transcripts for a RNA transcript that corresponds to said selected portion of said selected DNA molecule via the incorporation of a labeled precursor into the amplification process(Col. 6 lines 4-6 and Col. 8 lines 47-67 for example),

(C) repeating (A) and (B) on at least one other selected portion of said selected DNA molecule(Col. 3 lines 26-58, where the reference teaches that a "plurality of copies of the RNA sequence of the first template from the third template" can be synthesized).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davey et al. (US Patent 5,409,818) in view of Wittwer et al.(US Patent 6,503,720 B2).

With regard to claims 13 and 16 Davey et al. teach a method for determining whether a selected DNA molecule encodes a gene expression region which in this case is a 92 bp segment of the gag portion of the HTLV-III genome, the causative agent of AIDS(Col. 12 lines 33-35), said method comprising:

(A) obtaining RNA transcripts from an organism(ultimately HIV-1 virus, also *E.Coli*, Col. 11 line 50) which comprises said selected DNA molecule,

(B) screening said RNA transcripts for an RNA transcript corresponding to a selected portion of said selected DNA molecule, wherein the nucleotide sequence of said selected portion of said selected DNA molecule is known, to thereby determine whether said selected portion of said selected DNA molecule encodes a gene expression region such as the 92 bp segment of the gag portion of the HTLV-III genome(Col. 12 lines 33-35), wherein said screening comprised:

(i) amplifying the RNA transcripts using a first oligonucleotide primer and a second oligonucleotide primer, wherein said first primer is complementary to a sequence of at least 10 continuous nucleotides located at or near the 3'-end of said selected portion of said selected portion of said selected DNA molecule, and said second primer is homologous to a sequence of at least 10 continuous nucleotides located at or near the 5'-end of said selection portion of said selected DNA molecule(See Figure 1 and Col. 5 lines 14-25, Col. 6 lines 19-68 for example), and

(a) forming a RNA-DNA duplex comprising one of said RNA transcripts and a complementary DNA molecule adhered thereto, said duplex is formed by synthesizing a first DNA molecule complementary to at least a portion of one of said RNA transcripts using (1) said first oligonucleotide primer to prime synthesis of said first DNA molecule, (2) RNA-dependent DNA polymerase and (3) one of said RNA transcripts as a template, to thereby form an RNA-DNA duplex as can be seen in Figure 1 and Col. 5 lines 27-35 for example.

(b) preparing a single stranded DNA molecule from said RNA-DNA duplex of (e) by hydrolyzing the RNA transcript of said RNA-DNA duplex using ribonuclease H(Col. 8 lines 20-33 for example).

(c) forming a doubled-stranded DNA molecule comprising the single-stranded DNA molecule of (f) and a complementary DNA molecule thereto, said doubled-stranded DNA molecule is formed by synthesizing a second DNA molecule complementary to at least a part of said single-stranded DNA molecule of (f) using (1) said second oligonucleotide primer to prime the synthesis of said second DNA molecule, wherein said second primer further comprises an RNA-transcriptable promoter sequence at its 5'-end, (2) DNA-dependent DNA polymerase, and (3) the single-stranded DNA molecule of (f) as a template, to thereby form a double stranded DNA molecule as can be seen in Figure 1 and further in Col. 4 lines 10-15.

(d) forming an RNA transcription product from said double-stranded DNA molecule of (g) using RNA polymerase, wherein RNA transcription is primed from the RNA-transcriptable promoter sequence(Col. 7 lines 28-47 for example).

(e) repeating steps (a) to (d) using said RNA transcription product of (d) as a template for the formation of the RNA-DNA duplex of (a)(Col. 19 claim 1(C)).

(ii) detecting an amplification product of (i) corresponding to said selected portion of said DNA molecule, to thereby screen said RNA transcripts for an RNA transcripts for a RNA transcript that corresponds to said selected portion of said selected DNA molecule via the incorporation of a labeled precursor into the amplification process(Col. 6 lines 4-6 and Col. 8 lines 47-67 for example),

(C) repeating (A) and (B) on at least one other selected portion of said selected DNA molecule(Col. 3 lines 26-58, where the reference teaches that a "plurality of copies of the RNA sequence of the first template from the third template" can be synthesized).

With respect to claim 14 step (i), in Col. 9 lines 23-27 Davey et al. teaches that a preferred embodiment includes a probe with a corresponding sequence derived from that part of the selected portion of a specific nucleic acid sequence which is between the sequences of the first primer and the second primer, therefore teaching a probe that is not complementary to either the first or second oligonucleotide primers.

But, with regard to claims 14 and 15, Davey et al. do not teach all of step (c) specifically wherein said probe is labeled with an intercalating fluorescence dye and with respect to claim 15 an intercalating fluorescence dye that has a differential fluorescence characteristic depending on whether said probe exists in an unbound single-stranded state or in a bound duplex with said amplification product.

However, Wittwer et al.(US Patent 6,503,720 B2) teach such an intercalating probe in their teaching of amplification by PCR and subsequent detection with SYBR green in Example 2, Col. 9-10 and further teach an intercalating fluorescence dye that has a differential fluorescence characteristic depending on whether said probe exists in an unbound single-stranded state or in a bound duplex with said amplification product in Col. 7 lines 6-19 for example when they assert that using their Taq Man principle detects an amplification product, which is labeled with a fluorescent entity, the fluorescence emission of which is quenched by a second label in its un-hybridized form and upon its hybridization to its target sequence and following digestion with a DNA polymerase having a 5'-3' exonuclease activity, lacks quencher and therefore fluoresces in its hybridized state as compared to its un-hybridized form. In addition, in Col. 4 lines 7-10, Wittwer specifically teaches that "within the scope of the invention, are different methods for amplifying nucleic acids, for example NASBA(WO

91102814)" which applicant themselves teach in their specification on page 11 line 6 and further in their examples as an embodied method of RNA amplification.

Therefore, It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of Davey et al. with the use of SYBR Green, intercalating based fluorescent probes of Wittwer et al. for the expected benefit derived from the Wittwer et al. probe that allows for the concentration of an amplifiable or replicable analyte being determined without correction for different fluorescent backgrounds (Col. 2 lines 22-24) and further "provides such an independence of absolute signal level for systems wherein multiple fluorescent signals being detected through multiple channels with different window ranges may be compared"(Col. 2 lines 30-34). Furthermore, the motivation to combine the two references existed since Davey's 3SR method of RNA amplification(also know as NASBA) was taught by Wittwer et al. to be "within the scope of the invention" as it is a "different method for amplifying nucleic acids, for example NASBA(WO 91102814)" as taught by Wittwer et al. in Col. 4 lines 7-10.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sally A. Sakelaris whose telephone number is 571-272-0748. The examiner can normally be reached on M-Fri, 9-6:30 1st Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 571-272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sally Sakelaris

10/13/2005

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